REMARKS

Claims 13-16, 20-22, 30, 43-60 and 62-68 presently appear in this case. No claims have been allowed. The Official Action of May 8, 2001, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to cDNA sequences which encode polypeptides that bind to TRAF2 and modulate activity of NF-κB as well as the polypeptides encoded by those DNA sequences. Preferably, the polypeptide is NIK. The invention also relates to antibodies, methods of identification and screening ,and antisense DNA.

It is noted that the Examiner has withdrawn the allowability of claims 13-16, 20, 30, 43-49, 51-58, 60 and 62-63, in order to make a new rejection under 35 U.S.C. 112, first paragraph. It is further noted that the Examiner has acknowledged applicant's Request for Interference. However, prosecution in the instant application continues since no claims stand allowable.

Claims 13-16, 20-22, 30, 43-60, and 62-68 have been rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for polypeptides which inhibit or increase the expression of NF-κB does not reasonably provide enablement for polypeptides which "both inhibit and

increase (i.e., modulate) the expression of NF-κB." The Examiner states that the specification as filed does not provide sufficient guidance and/or instruction that would teach one of skill in the art how to isolate a polypeptide which binds TRAF2 and which "both inhibits and increases (i.e., modulate) the expression of NF-κB activity." The Examiner states that the exemplified polypeptides do not both inhibit and increase the activity of NF-κB. This rejection is respectfully traversed.

It is apparent that the present rejection is based on the Examiner's interpretation of the word "modulate" to mean "both inhibits and increases". This was not the intended meaning of "modulate" as appearing in the claims, and it is believed that those of ordinary skill in the art would understand that the term should be given its ordinary meaning, i.e., it either inhibits or increases the activity of NF-κB. Nevertheless, to obviate this rejection and in view of the Examiner's statement that the present claims are enabling for polypeptides which inhibit or increase the expression of NF-κB, all of the claims have now been amended to delete the term "modulate" and to substitute "either inhibits or increases", where appropriate, and to change the term "the cellular activity modulated/mediated by a polypeptide..." to read

"cellular activity which is changed or mediated by a polypeptide..."

In view of the elimination of the term "modulate" and the substitution of language which the Examiner advises is enabled by the specification, it is believed that this rejection is now been obviated. Reconsideration and withdrawal thereof is therefore respectfully urged.

The present amendment is accompanied by a substitute specification. In accordance with 37 C.F.R. §1.125(b)(1), applicant hereby states that the substitute specification includes no new matter. In accordance with 37 C.F.R. §1.125(b)(2), a marked up version of the substitute specification showing all the changes (including the matter being added to and the matter being deleted) to the specification of record is also attached hereto.

The present substitute specification will facilitate the interference proceeding if applicant's Request for Interference is granted. It has been noted that some errors occur in the sequences of the drawings. Corrected drawings are in the course of being prepared and will be filed as a supplemental amendment. As soon as the corrected specification and drawings are approved, an electronic copy of the application will be filed for early publication.

In view of the fact that the sole remaining rejection of the claims has now been overcome, the present claims should stand allowable. Accordingly, it is requested that applicant's Request for Interference filed February 9, 2001, be considered and granted.

It is submitted that all the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned "Version with markings to show changes made".

It is submitted that all the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

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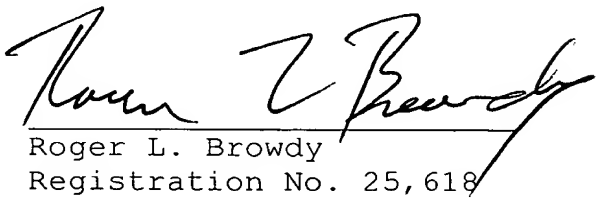
By 
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Version with Markings to Show Changes Made

Claims 21, 30, 45-49, 51, 59, 60, 62, 64 and 68 have been amended as follows:

21 ~~(Twice-amended)~~ (Thrice-amended). A method for producing a polypeptide that binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB, comprising:

growing transformed host cells in accordance with claim 16 under conditions for the expression of an expression product from said cells;

effecting post-translational modification of said expression product as necessary for obtaining said polypeptide; and

isolating said polypeptide.

30 (Amended). A method for isolating and identifying a polypeptide, according to claim 20, capable of binding directly to TRAF2, comprising applying the yeast two-hybrid procedure in which a sequence encoding said TRAF2 is carried by one hybrid vector and a sequence from a cDNA or genomic DNA library is carried by the second hybrid vector, the vectors then being used to transform yeast host cells and the positive transformed cells being isolated, followed by

extraction of the said second hybrid vector to obtain a sequence encoding a protein which binds to said TRAF2.

45 (Amended). A method for identifying and producing a ligand capable of ~~modulating~~either inhibiting or increasing the cellular activity ~~modulated~~/which is changed or mediated by TRAF2 comprising:

a) screening for a ligand capable of binding to a polypeptide comprising at least a portion of TRAF2 having the amino acid residues 222-501 of TRAF2;

b) identifying and characterizing a ligand, other than TRAF2 or portions of a receptor of the TNF/NGF receptor family, found by the screening of (a) to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

46 ~~(Twice-amended)~~ (Thrice-amended). A method for identifying and producing a ligand capable of ~~modulating~~either inhibiting or increasing the cellular activity ~~modulated~~which is changed or mediated by a polypeptide according to claim 53, comprising:

a) screening for a ligand capable of binding to said polypeptide;

b) identifying and characterizing a ligand, other than TRAF2 or portions of a receptor of the TNF/NGF receptor

family, found by said screening to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

47 (Amended). A method for identifying and producing a ligand capable of ~~modulating~~either inhibiting or increasing the cellular activity ~~modulated/~~which is changed or mediated by NIK comprising:

a) screening for a ligand capable of binding to at least a portion of the NIK sequence of SEQ ID NO:7;

b) identifying and characterizing a ligand, other than TRAF2 or portions of a receptor of the TNF/NGF receptor family, found by said screening step to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

48 (Amended). A method for identifying and producing a molecule capable of directly or indirectly ~~modulating~~either inhibiting or increasing the cellular activity ~~modulated/~~which is changed or mediated by NIK, comprising:

a) screening for a molecule capable of ~~modulating~~either inhibiting or increasing activities ~~modulated/~~which is changed or mediated by NIK;

b) identifying and characterizing said molecule; and

c) producing said molecule in substantially isolated and purified form.

49 (Amended). A method for identifying and producing a molecule capable of directly or indirectly ~~modulating~~either inhibiting or increasing the cellular activity ~~modulated/~~which is changed or mediated by a polypeptide according to claim 51;

b) identifying and characterizing said molecule; and

c) producing said molecule in substantially isolated and purified form.

51 (Amended). A polypeptide that binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB, said polypeptide comprising:

a) the amino acid sequence of SEQ ID NO:2, an amino acid sequence encoded by the nucleotide sequence of SEQ ID NO:6, or the amino acid sequence of SEQ ID NO:5;

b) an amino acid sequence of a fragment of a), which fragment binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB;

c) an amino acid sequence of an analog of a) or b), having no more that ten changes in the amino acid sequence of a) or b), each said change being a substitution, deletion or insertion of an amino acid, which analog binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB; or

d) a derivative of a), b) or c) which binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB.

55 (Amended). A DNA sequence encoding a polypeptide that binds to TRAF2 and ~~modulates~~either inhibits or increases activity of NF-κB, selected from the group consisting of

(i) a cDNA sequence comprising the nucleotide sequence of SEQ ID NO:1;

(ii) a cDNA sequence comprising the nucleotide sequence of SEQ ID NO:6;

(iii) a cDNA sequence comprising the nucleotide sequence of SEQ ID NO:4;

(iv) a fragment of a sequence of (i)-(iii) which encodes a polypeptide that binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB;

(v) a DNA sequence capable of hybridization to a sequence of (i)-(iv) under moderately stringent conditions and which encodes a polypeptide that binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB; and

(vi) any DNA sequence other than those defined in (i)-(v) which encodes a polypeptide in accordance with claim 51.

59 ~~(Twice-amended)~~ (Thrice-amended). A DNA sequence encoding

(1) a polypeptide in accordance with claim 53, or

(2) a polypeptide that binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB and is encoded by a DNA sequence capable of binding to a DNA sequence encoding the sequence of (1) under moderately stringent conditions.

60 (Amended). An anti-sense oligonucleotide consisting of a sequence complementary to at least a portion of the mRNA encoding a TRAF2-binding polypeptide comprising the amino acid sequence of SEQ ID NO:2, an amino acid sequence encoded by the nucleotide sequence of SEQ ID NO:3, or the amino acid sequence of SEQ ID ~~nO~~NO:5, said anti-sense

oligonucleotide being capable of effectively blocking the translation of said mRNA.

62 (Amended). An isolated polypeptide comprising the amino acid sequence set forth as SEQ ID NO:7 or an analog thereof which differs from the sequence of SEQ ID NO:7 by a substitution, deletion or insertion of a single amino acid, which analog binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB.

64 (Amended). A method for identifying and producing a ligand capable of ~~modulating~~either inhibiting or increasing the cellular activity ~~modulated~~which is changed or mediated by a polypeptide according to claim 62, comprising:

a) screening for a ligand capable of binding to said polypeptide;

b) identifying and characterizing a ligand, other than TRAF2 or portions of a receptor of the TNF/NGF receptor family, found by said screening to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

68 ~~(Amended)~~ (Twice-amended. A method for producing a polypeptide that binds to TRAF2 and ~~modulates~~either inhibits or increases the activity of NF-κB, comprising:

growing transformed host cells in accordance with claim 67 under conditions for the expression of an expression product from said cells;

effecting post-translational modification of said expression product as necessary for obtaining said polypeptide; and

isolating said polypeptide.